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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/797,952

03/11/2004

Marina Lowen

SHLI-038-002

4856

22428 7590 03/16/2007  
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EXAMINER

AFREMOVA, VERA

ART UNIT

PAPER NUMBER

1657

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/16/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/797,952	LOWEN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 8-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1-6 is/are allowed.
- 6) ☐ Claim(s) 7 and 16-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-7 and 16-21 as amended (1/03/2007) are under examination.

This application contains claims 8-15 drawn to an invention nonelected with traverse in paper(s) filed 8/15/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Specification***

The disclosure is objected to because of the following informalities:

This application contains Figure 1 but the section "BRIEF DESCRIPTION OF THE DRAWING (S)" is missing. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 as presently amended is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 as being depended on the amended claim 1 now extends rather than further limits the claimed invention by the virtue of the claim language "comprises". It is suggested to write, for example: "wherein the concentration of ... (ingredient) is ... (amount)" as related to each claimed ingredient of the presently claimed composition limited by the language "consisting essentially of" (claim 1).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16 and 17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yamashita et al. ("New and better protocols for a short-term Caco-2 cells culture system". Journal of Pharmaceutical Sciences. March 2002. Vol. 91, No. 3, pages 669-679) in the light of evidence by Barka et al. (Journal of Histochemistry and Cytochemistry. Novembre 2000. Vol. 48, pages 1453-1460.).

Claims are directed to a method of making a composition for culturing intestinal epithelial cells by mixing a cell culture medium composition with supplements including serum, non-essential amino acids, transferrin, insulin, epithelial growth factor (EGF), butyrate, hydrocortisone, progesterone and testosterone. Some claims are further drawn to incorporation of non-essential amino acids (NEAA) at concentration 1% in the medium and to incorporation of fetal bovine serum in amounts 5-20% in the medium.

The reference by Yamashita et al. teaches a culture system for culturing intestinal epithelial cells that combines basic culture medium BCM, differentiation medium DM and butyrate (page 671, table 1, protocol). The BCM includes DMEM supplemented with 1% NEAA and 10% FBS (page 670, col. 1, par. 3). The DM contains MITO extender (page 671, col. 2). The MITO extender contains transferrin, insulin, epithelial growth factor (EGF), hydrocortisone, progesterone and testosterone as evidenced by Barka et al. (see section materials and methods).

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Thus, the whole culture system made by combining or admixing ingredients during culturing protocols practiced under sterile conditions is considered to be a method of making composition by admixing ingredients under sterile conditions within the meaning of the claims.

Thus, the reference by Yamashita et al. anticipates the claimed invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7 and 16-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yamashita et al. ("New and better protocols for a short-term Caco-2 cells culture system". Journal of Pharmaceutical Sciences. March 2002. Vol. 91, No. 3, pages 669-679), Barka et al. (Journal of Histochemistry and Cytochemistry. Novembre 2000. Vol. 48, pages 1453-1460) and US 5,712,163 (Parenteau et al.).

Claims are directed to a composition for culturing intestinal epithelial cells and to a method of making a composition for culturing intestinal epithelial cells wherein the composition comprising a cell culture medium, serum, non-essential amino acids, transferrin, insulin, epithelial growth factor (EGF), butyrate, hydrocortisone, progesterone and testosterone. Some claims are/are further drawn to incorporation of non-essential amino acids (NEAA) at concentration 1% in the medium and to incorporation of fetal bovine serum in amounts 5-20% in the medium. Some claims are/are further drawn to the use of particular concentrations of transferrin, insulin, epithelial growth factor (EGF), butyrate, hydrocortisone, progesterone and

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testosterone in the culture system for culturing epithelial cells.

The reference by Yamashita et al. teaches a culture system composition for culturing intestinal epithelial cells that comprises a basic cell culture medium DMEM, serum, non-essential amino acids, butyrate, transferrin, insulin, epithelial growth factor (EGF), hydrocortisone, progesterone and testosterone as evidenced by the reference by Barka et al. as well as some other components.

The references by Yamashita et al and by Barka et al. are silent about concentration of some supplements and hormones. However, US 5,712,163 teaches culture media and culture systems for epithelial cells comprising supplements such as transferrin, insulin, EGF and hormones including hydrocortisone and progesterone at concentrations within the presently claimed ranges (column 5, lines 25-60; column 17, lines 25-30; column 19, lines 25-43). Thus, the use of particular concentrations as encompassed by the presently claimed invention is obvious as intended for making culture composition and/or kit for culturing epithelial cells including intestinal epithelial cells.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to include supplements and hormones at concentrations as required by the present invention with a reasonable expectation of success in making a culture composition suitable for growth and differentiation of for epithelial cells as adequately suggested by the prior art of record. One of skill in the art would have been motivated to combine known components at their suggested concentrations for the expected benefits in culturing and differentiation epithelial cells for the expected benefits in producing cells suitable for grafting

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and for testing pharmaceuticals. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

### ***Response to Arguments***

Applicant's arguments filed 1/03/2007 have been fully considered but they are not persuasive with respect to the presently rejected claims for the reason above.

Rejection(s) of claims 1-6 over the prior art has been withdrawn in view of applicants arguments that the ingredients in the cited references which are not listed in the instant claims by the virtue of the phrase "consisting essentially of" would not effect the effects of the claimed medium composition as intended for epithelial cell model (response page 6, par. 1 and page 7, par. 2-3). The claimed invention recited in claims 7 and 16-21 is open to incorporation of additional components disclosed in the cited references.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1657

March 14, 2006

A handwritten signature in black ink, appearing to read 'V. Afremova', with a horizontal line extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER